

**Remarks**

Claims 1, 2, 5, 9-16, 18-20 and 24-29 are pending. No new matter has been added.

***Rejection under 35 U.S.C. § 103***

Claims 1, 2, 5, 9-16, 18-20 and 24-29 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 99/15629 “in view of the known fact disclosed in the Specification on page 11, lines 9-26 and US Patent 6,830,927”. Applicant respectfully traverses.

At the outset, Applicant notes an apparent typographical error in the present Office Action. The Examiner states on page 2 paragraph 5 that “WO ‘629 teaches a method for in vitro culture of hematopoietic progenitor cells to produce differentiated cells of non-hematopoietic lineage” (emphasis added) and cites the document in its entirety and particularly the abstract as the source of this statement. For the record, Applicant notes that neither the abstract nor the remainder of the reference teaches such a method. Rather the reference teaches, inter alia, a method for in vitro culture of hematopoietic progenitor cells to produce differentiated cells of hematopoietic lineage. Applicant requests clarification.

WO 99/15629 teaches, inter alia, a method for in vitro culture of hematopoietic progenitor cells. This method enhances survival, maintenance and/or expansion of hematopoietic progenitor cells in their pluripotent state. WO 99/15629 also teaches a method for in vitro differentiation of hematopoietic progenitor cells into hematopoietic lineage-restricted progeny. The reference teaches that hematopoietic progenitor cells are immature blood cells that have the ability to differentiate into mature blood cells and can be obtained from blood products. (See page 14 lines 6-16.) The reference teaches the hematopoietic stem cells can be maintained in vitro in the absence of exogenous growth factors. It further teaches hematopoietic growth factors that promote differentiation of the cells into hematopoietic lineages. WO 99/15629 does not disclose a method of differentiating hematopoietic progenitor cells into cells of non-hematopoietic lineage.

U.S. Patent 6,830,927 teaches a method for in vitro culture of neuroepithelial (NEP) stem cells. The reference also teaches a method for in vitro differentiation of NEP cells into nervous system lineages. NEP cells differentiate into various lineages of the central and peripheral nervous systems, including neurons, glia, oligodendrocytes, astrocytes, and neural crest stem cells. These cell

are derived from caudal neuroepithelium, and they express nestin. NEP cells require FGF, but not EGF, and unknown components of chick embryo extract (CEE) to proliferate and self renew in culture, and NEP cells differentiate into neural crest stem cells in the presence of FGF, EGF, NGF and CEE together.

A prima facie case of obviousness requires showing (1) a motivation or suggestion to combine the cited references, (2) a reasonable expectation of success, and (3) that the combination results in each and every limitation of the pending claims. The Examiner has not made a prima facie case for the reasons set forth below.

There is no motivation or suggestion to combine the cited references at least because the references teach different progenitor populations. According to the references as discussed above, these progenitor populations differ with respect to their location in vivo, their differentiative profile, and their growth factor responsiveness. For example, WO 99/15629 teaches that its progenitors differentiate into hematopoietic cell lineages while US Patent 6,830,927 teaches that its progenitor differentiate into nervous system lineages. WO 99/15629 does not contemplate that its progenitors are able to differentiate into any lineages other than hematopoietic lineages, and similarly US Patent 6,830,927 does not contemplate that its progenitors are able to differentiate into any lineages other than hematopoietic lineages.

The Examiner states that it would have been obvious to “apply the teaching of US Patent ‘927 and the known fact disclosed in the specification on page 11, lines 9-26 to those of WO ‘629” to obtain the claimed method. The Examiner further states that one of ordinary skill would have been motivated to combine the references “because growth differentiation condition (sic) wherein said conditions comprising bFGF and EGF were well known in the art and used to produce neuronal cells to taught by the known fact disclosed on page 11 and US Patent ‘927”.

The specification teaches on page 11, lines 9-26 a number of growth factors that can be used in the invention. These factors include but are not limited to bFGF and EGF. This passage also states that these factors were well known to those of ordinary skill in the art and that most were commercially available. Accordingly, the passage is read as disclosing the factors to be used when culturing hematopoietic progenitor cells to produce non-hematopoietic progeny.

The Examiner's reliance on this passage is unclear. An obviousness rejection must be based on the teachings of the prior art and not on the teachings within the instant specification. The Examiner must consider the prior art as if he has never read the instant specification. To do otherwise would be to engage in impermissible hindsight. Thus the Examiner's reliance on the specification and its combination with the prior art is improper.

The Examiner further relies on In re Sernaker to support the combination of the references. In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). The Examiner cites the case for the proposition that the "strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination." Id., MPEP 2144. However, Applicant notes that the actual teaching in the case is that "it is not necessary that the prior art suggest expressly or in so many words, the "changes or possible improvements" the inventor made. It was only necessary that he apply "*knowledge clearly present in the prior art.*" Sheckler, 438 F.2d at 1001, 168 USPQ at 717. (Emphasis supplied.) If this last test is not met, the invention claimed would not have been obvious from the references." Id. at 217. Applicant maintains that the prior art in the instant case does not provide such knowledge. Nothing in the cited art teaches the use of neural differentiation conditions in cultures of hematopoietic progenitor cells. Nothing in the cited art teaches that neural differentiation from hematopoietic progenitor cells is even possible. Applicant further notes that, using the standard referred to above, the Court in In re Sernaker reversed the Board's determination of obviousness.

Finally, if there is no motivation or suggestion to combine the references, there is also no requisite reasonable expectation of success.

In view of the foregoing, Applicant submits that a prima facie case has not been made, and the claimed invention is not rendered obvious by the prior art.

Reconsideration and withdrawal of the rejection is respectfully requested.

**Conclusion**

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, which is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

If the Examiner has any questions and believes that a telephone conference with Applicant's representative would prove helpful in expediting the prosecution of this application, the Examiner is urged to call the undersigned at (617) 646-8266.

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Respectfully submitted,



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